

### Abstract of the Disclosure

A universal tag assay is disclosed wherein at least one invasive cleavage reaction (ICR) is used to generate tagged molecules having identifier tags corresponding to target nucleotide sequences, and further wherein hybridization of any tagged molecule with a complementary detection probe on a universal detector indicates the presence of the corresponding target in the sample being assayed. Preferred embodiments include the use of ICR to generate molecules suitable for use in the universal tag assay to detect variant nucleotide sequences including single nucleotide polymorphisms (SNPs), allelic variants, and splice variants. Hybridization of tagged molecules to detection probes is preferably detected by electrochemical readout, in particular the use of ruthenium amperometry to detect hybridization of identifier tags to detection probes immobilized on a universal detector, preferably a universal chip having gold or carbon electrodes.